REMARKS

Entry of the Amendment is respectfully requested. Applicants submit the Amendment places the application in condition for allowance and raises no issues not previously considered by the Examiner.

Claims 1, 5, 16, and 19 have been amended to further clarify the invention. Claims 22-24 are newly presented. After entry of the Amendment, claims 1-3, 5, 6, 9, 10, and 16-24 will be pending.

Applicants submit new claims 22-24 are supported throughout the specification, including at page 9, lines 14-18, and raise no issues of new matter.

Enablement

Claims 1-3, 5, 6, 9, 10, and 16-21 were rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement. Applicants respectfully traverse this rejection.

Without acquiescing to the rejection and solely to expedite prosecution, Applicants have directed the claims to biografts comprising cardiomyocytes, methods of preparing biografts comprising cardiomyocytes, and methods of repairing myocardium with biografts comprising cardiomyocytes. Applicants reserve the right to pursue the canceled subject matter in a continuation application.

The Examiner acknowledges the scope of enablement includes fetal cardiomyocytes without any limitation to origin and autologous cardiomyocytes. The Examiner, however, alleges the specification does not enable matrices comprising syngeneic, allogeneic, or xenogeneic cells. The Examiner asserts the specification does not provide any guidance as to measures or methods necessary to prevent destructive allogeneic or xenogeneic immune responses following transplantation of matrices containing allogeneic or xenogeneic tissue. Applicants do not agree.

An enabling disclosure by definition turns on the objective understanding of a skilled artisan. Therefore, the enablement requirement can be met by reference to the knowledge of one of ordinary skill in the relevant art. *Bayer AG v. Schein Pharmaceuticals*, 301 F3d 1306, (Fed Cir. 2002); MPEP § 2164.08. At the time of filing, mechanisms of immune response and transplant rejection were known and the use of immunosuppressive drugs to prevent rejection of

transplanted tissue was a standard clinical treatment known to one of skill in the art. See, for example, Superdock and Helderman, 1993, *Sem. Resp. Infect.*, 8:52-159 (copy enclosed) at page 152:

> Advances in immunology, tissue, typing, and pharmaceuticals have had a dramatic impact on success rates and have allowed the successful transplantation of organs between genetically non-identical people...As transplantation has become so successful in the treatment of end-stage renal disease, organ transplantation has now become a form of replacement therapy for end-stage liver, lung, heart, and bond marrow disease. In addition, pancreatic transplantation is now an accepted therapy for insulin-dependent diabetes mellitus.

Superdock and Helderman, for example, disclose the use of azathioprine, gluccocorticoids, cyclosporine A, cyclosporine G, FK506, rapamycin, mycophenolic acid, mycophenolate mofetil (RS-61443), mizoribine, brequinar sodium, and deoxyspergulaine as immunosuppressants for long-term management of transplant recipients and discuss the immunosuppressant mechanisms of these immunosuppressive agents.

Woodley et al., 1990, *Heart Transplantation*, 8:83-96 (copy enclosed), for example, teach phases of immunosuppression associated with cardiac transplantation, an algorithmic approach to cardiac allograft rejection and treatment regime (Figure 4 at page 92), use and dosages of immunosuppressive agents, such as cyclosporine, azathioprine, corticosteroids, ATG/ALG, monoclonal antibody OKT3, vincristine, and methotrexate, for early prophylaxis, chronic maintenance, and rejection treatment (Table 1 at page 85, Figure 2 at page 86, and Figure 3 at page 87), pharmacology of the immunosuppressive agents including route of administration, side effects, and drug interactions (Table 2 at page 85), and mechanism of action of the immunosuppressive agents (Table 3 at page 86).

In view of the forgoing, Applicants submit one of skill in the art would have been able to make and use biografts comprising syngeneic, allogeneic, or xenogeneic cells without undue experimentation. Withdrawal of the rejection is respectfully requested.

Conclusion

In light of the forgoing Amendment and Remarks, Applicants' assert the claims are in condition for allowance. Early notice of allowable claims is requested. The Examiner is invited to telephone the undersigned attorney for clarification of any of these Remarks or Amendments, or to otherwise speed prosecution of this case.

Respectfully submitted,

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